REMARKS

Claims 40, 42, 43, 103, 111-143, and 145-153 are pending. Claims 42, 118, and 133 are rejected under 35 U.S.C. § 112, second paragraph, for indefiniteness. Claims 43, 127, 128, 133, and 135 are provisionally rejected for obviousness-type double patenting over claims 18 and 21 of copending U.S. Serial No. 09/993,739. Claims 40, 42, 43, 103, 111-118, 120, 127-131, 133, and 134 are rejected under 35 U.S.C. § 102(e) for anticipation by U.S. Patent No. 5,962,028 (hereinafter "the '028 patent"). Claims 40, 42, 43, 103, 111-114, 116-121, 124, 126-135, 138-140, 142, 143, 145, 146, 148, and 150-153 are rejected under 35 U.S.C. § 102(e) for anticipation by U.S. Patent No. 5,782,971 (hereinafter "the '971 patent"). Claims 40, 42, 43, 103, 111-118, 120-123, 125, 127-131, 133, and 134 are rejected under 35 U.S.C. § 103(a) for obviousness over the '028 patent. Claims 136, 137, 141, 147, and 149 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form. By this reply, Applicants amend claims 40, 42, 43, 103, 111, 118, 125, 129, 131, 133, 135, 138, and 146, and address each of the Examiner's rejections.

Support for the Amendment

Support for the amendment to claims 40, 43, and 103 is found in the specification on, e.g., page 21, lines 16-21, and page 61, line 4, through page 62, line 1. Support for the amendment to claim 111 is found in claim 111 as originally filed. Support for the amendment to claims 118, 133, and 138 is found in the specification on, e.g., page 20, line 23, though page 21, line 3, and page 51, lines 12-23. Support for the amendment to claims 135 and 146 is found in the specification on, e.g., page 38, lines 13-17. Claims 42 and 131 have been amended to correct

typographical errors. No new matter is added by the amendment.

Rejections Under 35 U.S.C. § 112, second paragraph

Claims 42, 118, and 133 are rejected under 35 U.S.C. § 112, second paragraph, for indefiniteness. The Examiner points out that "polyanhydrides" is recited twice in claim 42 and "it is unclear if copolymers are of poly(anhydride-co-imide) only, or of all the afore stated polymeric components" (Office Action, p. 5). Applicants have amended claim 42 to eliminate the duplication of "polyanhydrides" and to clarify that the "copolymers" refer to all of the polymeric compounds recited in the claim. Applicants also confirm that the "supplemental material" recited in claim 42 should be read to mean a compound or component selected from any of the groups listed, not as a compound or component selected from each group.

Claims 118 and 133 are rejected for reciting that the promoter can be "H_2PO_4," which is a phosphorous acid liquid, yet claims 40 and 43, upon which claims 118 and 133, respectively, depend, recite that the promoter is a powder. Applicants have amended claims 118 and 133 to recite that the promoter is "H_3PO_4," which is a solid. Thus, the rejection of claims 118 and 133 can now be withdrawn.

Claim 138, which was not rejected by the Examiner, has also been appropriately amended to replace "H_2PO_4" with "H_3PO_4."

Rejections under 35 U.S.C. § 102(e)

The '028 Patent

Claims 40, 42, 43, 111-118, 120, 127-131, 133 and 134 are rejected under 35 U.S.C. § 102(e) for anticipation by the '028 patent. The Examiner states that all of the elements of the rejected claims are disclosed by the '028 patent. Applicants respectfully disagree that the '028 patent teaches or suggests all of the elements of present claims 40, 42, 43, 111-118, 120, 127-131, 133 and 134.

M.P.E.P. § 2131 states: "'A claim is anticipated only if each and every element as set forth in the claims is found, either expressly or inherently described, in a single prior art reference.' *Verdegaal Bros. v. Union Oil Co. of California* 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)." For the reasons discussed below, the '028 patent fails to teach or suggest all of the limitations of present independent claims 40, 42, and 43, and claims dependent therefrom.

The '028 patent was characterized in the previous Reply to Final Office Action filed with the Request for Continued Examination on May 20, 2004. In brief, the '028 patent discloses carbonated hydroxyapatite compositions that are formed by mixing the dry ingredients (i.e., a phosphoric acid source, an alkali earth metal source, and a calcium carbonate) using mills or rollers "until a uniform dispersal of ingredients is obtained" (see, e.g., col. 4, lines 40-42, col. 5, lines 17-13, and col. 5, line 66, through col. 6, line 7). A lubricant is then added to the mixed dry ingredients in an amount to form a flowable "paste" or moldable "clay-like putty," which subsequently hardens (col. 6, lines 10-36). The '028 patent also discloses shaping the composition prior to, during, or after hardening of the paste or putty (i.e., after hydrating the dry powder component; see col. 7, lines 60-62).

Claim 40

Applicants first address the rejection as it applies to independent claim 40 and claims dependent therefrom. Independent claim 40, as presently amended, is directed to a method for preparing a bioceramic composition by dry mixing powders of a calcium phosphate and a promoter, pressing the dry powders (prior to hydration) to form a compressed object of predetermined shape, and hydrating the compressed powder object. The Examiner argues that because claim 40 is provided in open claim language, the "wet mixing" of powders disclosed by the '028 patent anticipates claim 40. Applicants have amended claim 40 to clarify that the mixing and compression of the powders occurs in the absence of hydration (i.e., "dry mixing"). The '028 patent simply fails to describe a step in which the dry ingredients are mixed and compressed to form a compressed object of predetermined shape *prior to hydration*. In fact, the '028 patent fails to teach or suggest the formation of any compressed powder objects in the absence of hydration. Because the '028 patent fails to teach or suggest the formation of a compressed powder object in the absence of hydration, the '028 patent fails to disclose each and every method step of independent claim 40, as presently amended. Accordingly, the rejection of claim 40, and claims dependent therefrom, under 35 U.S.C. § 102(e) over the '028 patent should be withdrawn.

Claim 42

The '028 patent also fails to teach or suggest each and every element of independent claim 42 and claims dependent therefrom. Independent claim 42, as presently amended, recites a

composite material that includes a strongly bioresorbable, poorly crystalline apatitic (PCA) calcium phosphate having a Ca/P ratio of less than 1.5, which is in contact with a supplemental material that is present in an amount effective to impart a characteristic selected from the group consisting of strength, resorption time, adherence, frictional characteristics, release kinetics, tensile strength, hardness, fracture toughness, elasticity, and imaging capability. Claim 42 has been amended to recite that the supplemental material is selected from a bioresorbable material selected from the group consisting of silk, demineralized bone matrix, hyaluronic acid and derivatives thereof, polyorthoesters, polyglycolic acid, polylactic acid, and copolymers thereof, polyesters of α-hydroxycarboxylic acids, poly(L-lactide) (PLLA), poly(D,L-lactide) (PDLLA), polyglycolide (PGA), poly(lactide-co-glycolide (PLGA), poly(D,L-lactide-co-trimethylene carbonate), and polyhydroxybutyrate (PHB), polyanhydrides, poly(anhydride-co-imide), and co-polymers thereof, and bioactive glass compositions; a non-bioresorbable material selected from the group consisting of dextrans, polyethylene, polymethylmethacrylate (PMMA), carbon fibers, polyvinyl alcohol (PVA), poly(ethylene terephthalate)polyamide, bioglasses, and calcium phosphates; a lubricant selected from the group consisting of silicone oil, polymer waxes, lipids, and fatty acids, a non-bioresorbable material, a lubricant, and a radiographic material. The '028 patent fails to teach or suggest that the carbonated dahllite composition contains any of the supplemental materials recited in present claim 42.

The Examiner states: "As to supplemental materials, hyaluronic acid derivatives, collagen is included [in the carbonated dahllite composition of the '028 patent]" (Office Action, p. 3). Applicants note that while the '028 patent does disclose collagen as an additional component that can be added to the carbonated dahllite composition, collagen is not recited in present claim 42.

Thus, the disclosure of collagen as an additional component by the '028 patent fails to render claim 42, and claims 152 and 153 dependent therefrom, anticipated. Hyaluronic acid, in contrast, which is recited in present claim 42, is not taught or suggested by the '028 patent as an additional component that can be added to the carbonated dahllite composition. The '028 patent merely discloses:

> Various additional components may be included during the formation of the carbonated hydroxyapatite, dahllite. Of particular interest are pharmacologically active agents, proteins, polysaccharides, or other biocompatible polymers, or the like. Of particular interest are proteins involved in skeletal structure such as different forms of collagen, especially Type I, fibrin, fibrinogen, keratin, tubulin, elastin, and the like, or structural polysaccharides, such as chitin. Pharmacologically active agents might include drugs that enhance bone growth, serve as a variety of cell growth factors, or act as anti-inflammatory or anti-microbial agents. Examples of such proteins might include but not be limited to: bone morphogenetic protein, cartilage induction factor, platelet derived growth factor, and skeletal growth factor. (See col. 6, line 61, through col. 7, line 5.)

Thus, the '028 patent fails to teach or suggest a strongly bioresorbable, poorly crystalline apatitic calcium phosphate containing hyaluronic acid, much less any of the other supplemental materials recited in present claim 42, and claims dependent therefrom. Because the '028 patent fails to teach or suggest all of the limitations of present claims 42, 152, and 153, the rejection of these claims under 35 U.S.C. § 102(e) over the '028 patent should be withdrawn.

Claim 43

Finally, independent claim 43, as presently amended, is directed to a bioceramic composition comprising dry powders of a calcium phosphate and a promoter that have been compressed to form a powder object having a predetermined shape. In contrast, the '028 patent discloses the mixing of dry ingredients using mills or rollers to obtain a uniform dispersal (see

col. 5, line 67, through col. 6, line 9), followed by the addition of a lubricant to hydrate the powder and form a flowable "paste" or moldable "clay-like putty," which subsequently hardens (col. 6, lines 10-36). Because the '028 patent fails to teach or suggest the preparation of a compressed powder object by mixing powders and compressing them into a predetermined shape prior to hydration, the '028 patent fails to teach or suggest all of the limitations of present claims 43, 125-137, and 151. Thus, the rejection of independent claim 43, and claims dependent therefrom, under 35 U.S.C. § 102(e) over the '028 patent should be withdrawn.

The '971 Patent

Claims 40, 42, 43, 103, 111-114, 116-121, 124, 126-135, 138-140, 142, 143, 145, 146, 148, and 150-153 are rejected under 35 U.S.C. § 102(e) for anticipation by the '971 patent. The Examiner states that all of the elements of the rejected claims are disclosed by the '971 patent. As is discussed in greater detail below, Applicants have amended independent claims 40, 42, 43, 103, and 138 to distinguish the present claims over the '971 patent. Applicants will discuss the rejection as it applies to each independent claim.

Claim 40

The '971 patent discloses the preparation of a calcium phosphate cement by combining:

> amorphous calcium phosphate, at least one additional calcium source, as well as a physiologically acceptable lubricant. Combination of the various components of the subject compositions produces a flowable, paste-like material capable of setting in vivo into a remodelable calcium phosphate, usually apatitic, product. Col. 2, lines 28-34.

The '971 patent further discloses testing the setting time of the calcium phosphate cement by

filling Teflon ring molds with the calcium phosphate *paste*, allowing the paste to set, and determining the time required for setting (col. 7, line 46, through col. 8, line 23). The '971 patent also discloses testing the compressive strength of the hardened calcium phosphate cement by packing the calcium phosphate paste into a compression die, allowing the paste to set, and pressure testing the hardened cement (Col. 8, lines 32-60). In both instances, the '971 clearly indicates that a hydrated calcium phosphate *paste* is added to the mold and allowed to set.

In contrast, as is discussed above, present claim 40 recites dry mixing powders of a calcium phosphate and a promoter, pressing the dry powders (prior to hydration) to form a compressed object of predetermined shape, and hydrating the compressed powder object. The '971 patent simply fails to describe a step in which the dry ingredients are mixed and compressed to form a compressed powder object of predetermined shape *prior to hydration*. In fact, like the '028 patent, the '971 patent fails to teach or suggest the formation of any compressed powder objects in the absence of hydration. Because the '971 patent fails to teach or suggest the formation of a compressed powder object in the absence of hydration, the '971 patent fails to disclose each and every method step of independent claim 40, as presently amended. Accordingly, the rejection of claim 40, and claims dependent therefrom, under 35 U.S.C. § 102(e) over the '971 patent should be withdrawn.

Claim 42

The '971 patent also fails to teach or suggest each and every element of present claim 42 and claims dependent therefrom. The Examiner states that the '971 patent discloses "[a] number of supplemental agents to enhance...characteristics inclusive of resorption time, strength and

other desirable properties [and] may include Ca sulfate...Particulate extenders are at col. 6, top – calcium sulfate; Demineralized bone is matrix Gla – protein" (Office Action, p. 4). Applicants respectfully disagree that the '971 patent teaches or suggests all of the limitations of present claims 42, 152, and 153.

Claim 42 has been amended to exclude calcium sulfate, and thus, the '971 patent can no longer serve as the basis for a rejection of claims 42, 152, and 153 under 35 U.S.C. § 102(e) based on this element. In addition, the '971 patent fails to teach or suggest a strongly bioresorbable, poorly crystalline apatitic calcium phosphate containing demineralized bone matrix, as is recited in present claim 42, based solely on the disclosure of matrix Gla-protein because these two materials are not the same. Matrix Gla-protein is 14-kD extracellular matrix **protein** of the mineral-binding Gla protein family, which can be further described as a γ-carboxyglutamic acid (Gla)–rich, vitamin K–dependent and apatite-binding protein. In contrast, demineralized bone matrix is a complex composition containing approximately 99% **non-protein** matrix components and only about 1% protein components; the components, many of which are unknown, are provided in a substantially impure form. Thus, demineralized bone matrix and matrix Gla-protein are not the same. Furthermore, the '971 patent only discloses the addition of:

> specific proteins of interest includ[ing] osteonectin, bone sialoproteins (Bsp), α-2HS-glycoproteins, bone Gla-protein (Bgp), matrix Gla-protein, bone phosphoglycoprotein, bone phosphoprotein, bone proteoglycan, protolipids, bone morphogenic protein, cartilage induction factor, platelet derived growth factor, skeletal growth factor, and the like. Col. 5, line 67, through col. 6, line 6; emphasis added.

The '971 patent only discloses the use of specific proteins, not a complex consisting of primarily non-protein components. Because the '971 patent fails to teach or suggest that the additive could

be demineralized bone matrix, a substantially impure, heterogeneous composition that consists of primarily non-proteinaceous components, the '971 patent fails to teach or suggest all of the elements of present claims 42, 152, and 153. Accordingly, the rejection of claims 42, 152, and 153 under 35 U.S.C. § 102(e) over the '971 patent should be withdrawn.

Claim 43

Claim 43, and claims dependent therefrom, also stand rejected under 35 U.S.C. § 102(e) over the '971 patent. As is discussed above, claim 43, as presently amended, is directed to a bioceramic composition comprising dry powders of a calcium phosphate and a promoter that have been compressed to form a powder object having a predetermined shape; the compressed powder object is not hydrated. In contrast, the '971 patent discloses the mixing of dry ingredients followed by hydration with a lubricant, specifically to produce a **flowable** composition (see, e.g., col. 6, lines 12-21). Because the '971 patent fails to teach or suggest the preparation of a compressed powder object formed in the absence of a liquid component, the '971 patent fails to teach or suggest all of the limitations of present claim 43, and claims dependent therefrom. Thus, the rejection of claim 43, and claims dependent therefrom, under 35 U.S.C. § 102(e) over the '028 patent should be withdrawn.

Claim 103

The '971 patent also fails to teach or suggest all of the limitations of present independent claim 103, and claims dependent therefrom. Independent claim 103, as presently amended, is directed to a method for treating a bone defect by introducing a compressed powder object at the

bone site. Claim 103 has been amended to clarify that the compressed powder object is prepared by compressing dry powders of a calcium phosphate and a promoter (in the absence of a liquid component). As is discussed above, the '971 patent fails to teach or suggest the preparation of a compressed powder object in the absence of a liquid component. For this reason, Applicants respectfully request withdrawal of the rejection of claim 103, and claims dependent therefrom, under 35 U.S.C. § 102(e) for anticipation by the '971 patent.

Claim 138

Independent claim 138, and claims dependent therefrom, also stand rejected for anticipation by the '971 patent. Independent claim 138, as presently amended, is directed to a method for preparing a bioceramic composition by mixing powders of a calcium phosphate and a promoter selected from calcium metaphosphate, dicalcium phosphate dihydrate, heptacalcium decaphosphate, calcium pyrophosphate dihydrate, poorly crystalline apatitic (PCA) calcium phosphate, calcium pyrophosphate, monetite, octacalcium phosphate, CaO, calcium acetate, H_3P0_4, and amorphous calcium phosphate in a hydrating medium to form a paste, introducing the paste into a mold that approximates a desired implant shape, and allowing the paste to harden into a PCA calcium phosphate article. The method of claim 138 yields a bioceramic implant composition which can be used by the skilled artisan to prepare an implant having the approximate size and shape needed to replace or repair a defect, e.g., a bone defect, in a patient; the skilled artisan would not have to mold the implant during surgery using, e.g., a moldable paste. The Examiner argues that the '971 patent anticipates claim 138, and claims dependent

therefrom, because the '971 patent discloses the use of a die to permit the formation of a predetermined, shaped article (Office Action, p. 3). Applicants respectfully disagree that the '971 patent teaches or suggests the method of present claim 138.

Applicants have amended claim 138 to clarify that the method requires the use of a mold that "approximates a desired implant shape." The '971 patent fails to teach or suggest this limitation. The '971 patent merely discloses the use of a mold or compression die for preparing a hardened calcium phosphate, which can be subsequently tested to determine its compression strength. The '971 patent fails to teach or suggest that the mold or compression die is used to prepare a calcium phosphate bioceramic implant composition having a desired shape for implantation or that one skilled in the art should use a mold that would allow the calcium phosphate paste to harden in a desired shape for implantation. Absent this teaching or suggestion, the '971 patent fails to teach or suggest all of the limitations of present claim 138, and claims dependent therefrom. For this reason, Applicants respectfully request that the rejection of claims 138-140, 142, 143, 145, 146, and 148 under 35 U.S.C. § 102(e) for anticipation by the '971 patent should be withdrawn.

Rejections under 35 U.S.C. § 103(a)

Claims 40, 42, 43, 103, 111-118, 120-123, 125, 127-131, 133, and 134 are rejected under 35 U.S.C. § 103(a) for obviousness over the '028 patent. The Examiner states that the '028 patent

> uses the instant components, mixed as powders, with lubricant fluids added to provide wet mixing, or added after mixing, followed by compression. There is no preclusion of the instant language of fluid with powder, since the instant language is in open guise, thus obvious over the

> same steps of [the '028 patent] regardless of when each step is performed, since the outcome, the product, is the same in each case. Office Action, p. 5.

As is discussed above, Applicants have amended independent claims 40, 43, and 103 to recite a compressed powder object prepared by compressing dry powders, thus precluding the presence of fluid. Therefore, the rejection of claims 40, 43, 103, 111-118, 120-123, 125, 127-131, 133, and 134 for obviousness over the '971 patent can now be withdrawn.

The '971 patent also fails to teach or suggest all of the limitations of independent claim 42, as presently amended, for the reasons discussed above. Namely, the '971 patent fails to teach or suggest a strongly bioresorbable, poorly crystalline apatitic calcium phosphate having any of the supplemental materials recited in present claim 42. Because the '971 fails to teach or suggest all of the limitations of present claim 42, the rejection of claim 42 for obviousness over the '971 patent can now be withdrawn.

Provisional Obviousness-type Double Patenting Rejections

The Examiner rejects claims 43, 127, 128, 133, and 135 for provisional obviousness-type double patenting over claims 18 and 21 of copending U.S. Serial No. 09/993,739. The Examiner states that "[a]lthough the conflicting claims are not identical, they are not patentably distinct from each other because the '739 application and [the] current application claim variants, obvious, of the same subject matter" (Office Action, p. 2).

Applicants will address the provisional obviousness-type double patenting rejection in the present case once otherwise allowable subject matter has been determined in this application.

CONCLUSION

In view of the above remarks, Applicants respectfully submit that the claims are in condition for allowance, and such action is respectfully requested.

Enclosed is a petition to extend the period for replying for three months, to and including June 17, 2005, and a check for the fee required under 37 C.F.R. § 1.17(a).

If there are any additional charges, or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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